

[Order File](#)**Dialog eLink:** [History](#)

**Transdermal-type formulation useful for treating and preventing frequent urination, asthma, chronic obstructive pulmonary disease and irritable bowel syndrome, comprises muscarine receptor antagonist in external base**

**Patent Assignee:** KYORIN PHARM CO LTD; KANAYAMA N; NAKASHIMA K; OHMORI S; SAKAI Y; ONO PHARM CO LTD

**Inventors:** KANAYAMA N; NAKASHIMA K; OHMORI S; SAKAI Y

#### Patent Family (4 patents, 107 countries)

Patent Number	Kind	Date	Application Number	Kind	Date	Update	Type
WO 2005011683	A1	20050210	WO 2004JP11068	A	20040803	200517	B
EP 1652523	A1	20060503	EP 2004748201	A	20040803	200629	E
			WO 2004JP11068	A	20040803		
US 20060188554	A1	20060824	WO 2004JP11068	A	20040803	200656	E
			US 2006566502	A	20060206		
JP 2005512547	X	20071004	WO 2004JP11068	A	20040803	200766	E
			JP 2005512547	A	20040803		

**Priority Application Number (Number Kind Date):** JP 2003286103 A 20030804

#### Patent Details

Patent Number	Kind	Language	Pages	Drawings	Filing Notes
WO 2005011683	A1	JA	35	4	

National Designated States,Original	AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW		
Regional Designated States,Original	AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW		
EP 1652523	A1	EN	PCT Application WO 2004JP11068 Based on OPI patent WO 2005011683
Regional Designated States,Original	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PL PT RO SE SI SK TR		
US 20060188554	A1	EN	PCT Application WO 2004JP11068 PCT Application WO 2004JP11068 Based on OPI patent WO 2005011683
JP 2005512547	X	JA	25

**Alerting Abstract:** WO A1

**NOVELTY** - A transdermal-type formulation comprises a muscarine receptor antagonist and an external preparation base.

**ACTIVITY** - Uropathic; Antiasthmatic; Respiratory-Gen.; Gastrointestinal-Gen.; Antiinflammatory. No

test details are given.

**MECHANISM OF ACTION** - Muscarine receptor antagonist; Parasympatholytic-M1; Parasympatholytic-M3. No test details are given.

**USE** - Useful for treating and preventing frequent urination, urinary incontinence with respect to the overactive bladder patient, asthma, chronic bronchial obstructive disease and irritable bowel syndrome (claimed).

**ADVANTAGE** - The transdermal preparation produce very little skin irritation. The muscarinic antagonist is continuously and efficiently absorbed into the body through the skin, thereby providing sustained efficacy with little side effects. The formulation is excellent in skin permeation of the muscarinic antagonist.

### **Technology Focus:**

**PHARMACEUTICALS** - Preferred Drug: The muscarine receptor antagonist is 4-(2-methyl-1-imidazolyl)-2,2-diphenyl butylamide, (-)-(R)-2-[(alpha)-[2-(diisopropyl amino)ethyl]benzoyl]-p-cresol tartrate, (S)-1-[2-(2,3-dihydro-5-benzo furanyl)ethyl]- (alpha), (alpha)-diphenyl-3-pyrrolidine acetamide hydrobromide, (+)-(1S,3'R)-quinuclidine-3'-yl-phenyl-1,2,3,4-tetrahydro isoquinoline-2-carboxylate succinate, 4-diethyl amino-2-butynyl(+/-)-alpha-cyclohexyl-(alpha)-phenyl glycolate hydrochloride, (+/-)-N-t-butyl-1-methyl-3,3-diphenyl propylamine hydrochloride and 2-piperidino ethyl-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carboxylate hydrochloride. The formulation contains soluble or insoluble type 4-(2-methyl-1-imidazolyl)-2,2-diphenyl butylamide as an active ingredient.

Preferred Form: The formulation is formulated as patch such as an adhesive monolayer type or reservoir type transdermal preparation. The monolayer type patch has a support and a peeling liner with an adhesion layer containing 4-(2-methyl-1-imidazolyl)-2,2-diphenyl butylamide and the external preparation base. The reservoir type patch consists of a drug penetration control film, an adhesion layer, a support and a peeling liner.

**ORGANIC CHEMISTRY** - Preferred Components: The external base comprises amphiphilic dissolution adjuvant, a suspensible base, a softener, an emulsifier, a buffer, a percutaneous transmission promoter, an adhesive, an adhesion enhancer, an adhesive agent, a skin irritation mitigator and/or an additive. The external preparation base further comprises a water-soluble polymer compound, a fat-soluble polymer compound, a fatty acid, fatty acid ester, fatty acid metal salt, animal and plant fats and oils, alcohol, a terpene type compound and/or water.

### **International Patent Classification**

<b>IPC</b>	<b>Level</b>	<b>Value</b>	<b>Position</b>	<b>Status</b>	<b>Version</b>
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## Dialog Results

A61F-0013/02	A	I	L	B	20060101
A61K-0031/4164	A	I	L	B	20060101
A61K-0031/4174	A	I	F	B	20000101
A61K-0031/4174	A	I		R	20060101
A61K-0031/445	A	I	F	B	20060101
A61K-0047/06	A	I	L	B	19900101
A61K-0047/06	A	I		R	20060101
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A61K-0009/70	A	I		R	20060101
A61P-0013/10	A	I	L	B	20000101
A61P-0013/10	A	I		R	20060101
C07D-0233/61	A	I	L	B	19850101
C07D-0233/61	A	I		R	20060101
A61K-0031/4174	A	I	L	B	20060101
A61K-0009/70	A	I	F	B	20060101
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A61P-0011/00	A	I	L	B	20060101
A61P-0011/06	A	I	L	B	20060101
A61P-0013/02	A	I	L	B	20060101
A61P-0043/00	A	I	L	B	20060101

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A61K-0031/4164	C	I		R	20060101
A61K-0031/4164	C	I	L	B	20060101
A61K-0031/445	C	I	F	B	20060101
A61K-0047/06	C	I		R	20060101
A61K-0047/10	C	I		R	20060101
A61K-0047/12	C	I		R	20060101
A61K-0047/14	C	I		R	20060101
A61K-0047/30	C	I		R	20060101
A61K-0047/44	C	I		R	20060101
A61K-0009/70	C	I		R	20060101
A61P-0013/00	C	I		R	20060101
C07D-0233/00	C	I		R	20060101
A61K-0031/4164	C	I		B	20060101
A61K-0009/70	C	I		B	20060101
A61P-0001/00	C	I		B	20060101
A61P-0011/00	C	I		B	20060101
A61P-0013/00	C	I		B	20060101
A61P-0043/00	C	I		B	20060101

**US Classification, Issued:** 424-448000

**US Classification, Issued:** 514-317000, 514-396000

**US Classification, Issued:** 424448, 514317, 514396

### Original Publication Data by Authority

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Publication Date: 20060503

\*\*TRANSDERMALES ABSORPTIONSPRAPARAT TRANSDERMAL ABSORPTION  
PREPARATION PREPARATION POUR ABSORPTION TRANSDERMIQUE\*\*

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Language: EN

Application: EP 2004748201 A 20040803 (Local application) WO 2004JP11068 A 20040803 (PCT Application)

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Related Publication: WO 2005011683 A (Based on OPI patent )

Designated States: (Regional Original) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PL PT RO SE SI SK TR

Original IPC: A61K-31/4174(B,I,H,EP,20000101,20050217,A,F) A61K-47/06(B,I,H,EP,19900101,20050217,A,L) A61K-47/10(B,I,H,EP,19900101,20050217,A,L) A61K-47/12(B,I,H,EP,19900101,20050217,A,L) A61K-47/14(B,I,H,EP,19900101,20050217,A,L) A61K-47/30(B,I,H,EP,19900101,20050217,A,L) A61K-47/44(B,I,H,EP,20000101,20050217,A,L) A61K-9/70(B,I,H,EP,19740701,20050217,A,L) A61P-13/10(B,I,H,EP,20000101,20050217,A,L) C07D-233/61(B,I,H,EP,19850101,20050217,A,L)

Current IPC: A61K-31/4174(B,I,H,EP,20000101,20050217,A,F) A61K-47/06(B,I,H,EP,19900101,20050217,A,L) A61K-47/10(B,I,H,EP,19900101,20050217,A,L) A61K-47/12(B,I,H,EP,19900101,20050217,A,L) A61K-47/14(B,I,H,EP,19900101,20050217,A,L) A61K-47/30(B,I,H,EP,19900101,20050217,A,L) A61K-47/44(B,I,H,EP,20000101,20050217,A,L) A61K-9/70(B,I,H,EP,19740701,20050217,A,L) A61P-13/10(B,I,H,EP,20000101,20050217,A,L) C07D-233/61(B,I,H,EP,19850101,20050217,A,L)

Current ECLA class: A61K-9/70E A61K-31/4174

Original Abstract: (Object) A transdermal preparation is provided, which ensures stable and effective absorption of 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197) which has a low skin absorption and is a bladder-selective muscarinic M3 and M1 receptor antagonist, into body through the skin while causing little side effects and providing sustained pharmacological effect with less skin irritancy. (Solving means) A composition comprising KRP-197 and an external preparation base is deposited and dried onto a structural body or a small pool of the composition is deposited on the structural body to obtain a single adhesive layer-type transdermal preparation or a reservoir-type transdermal preparation. These preparations can ensure high permeation of KRP-197 through the skin and sustained absorption of KRP-197 into body while causing decreased skin irritancy.

Claim: 1.A transdermal preparation containing a muscarinic receptor antagonist and an external preparation base.

## Japan

Publication Number: JP 2005512547 X (Update 200766 E)

Publication Date: 20071004

Language: JA (25 pages)

Application: WO 2004JP11068 A 20040803 (PCT Application) JP 2005512547 A 20040803 (Local application)

Priority: JP 2003286103 A 20030804

Related Publication: WO 2005011683 A (Based on OPI patent )

Original IPC: A61K-31/4164(B,I,M,98,20060101,20070907,C) A61K-31/4174(B,I,H,  
 JP,20060101,20070907,A,L) A61K-9/70(B,I,H,JP,20060101,20070907,A,F) A61K-9/70(B,I,  
 M,98,20060101,20070907,C) A61P-1/00(B,I,M,98,20060101,20070907,C) A61P-1/04(B,I,H,  
 JP,20060101,20070907,A,L) A61P-11/00(B,I,H,JP,20060101,20070907,A,L) A61P-11/00(B,I,  
 M,98,20060101,20070907,C) A61P-11/06(B,I,H,JP,20060101,20070907,A,L) A61P-13/00(B,I,  
 M,98,20060101,20070907,C) A61P-13/02(B,I,H,JP,20060101,20070907,A,L) A61P-43/00(B,I,H,  
 JP,20060101,20070907,A,L) A61P-43/00(B,I,M,98,20060101,20070907,C)

Current IPC: A61K-31/4164(B,I,M,98,20060101,20070907,C) A61K-31/4174(B,I,H,  
 JP,20060101,20070907,A,L) A61K-9/70(B,I,H,JP,20060101,20070907,A,F) A61K-9/70(B,I,  
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 JP,20060101,20070907,A,L) A61P-43/00(B,I,M,98,20060101,20070907,C)

## United States

Publication Number: US 20060188554 A1 (Update 200656 E)

Publication Date: 20060824

\*\*Transdermal absorption preparation\*\*

Assignee: Nakashima, Katashi, Tatebayashi-shi, JP Residence: JP Nationality: JP (NAKA-I) Ohmori, Satoshi, Tochigi-shi, JP Residence: JP Nationality: JP (OHMO-I) Kanayama, Norihiro, Tochigi, JP Residence: JP Nationality: JP (KANA-I) Sakai, Yoshiki, Osaka, JP Residence: JP Nationality: JP (SAKA-I)

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Language: EN

Application: WO 2004JP11068 A 20040803 (PCT Application) US 2006566502 A 20060206 (Local application)

Priority: JP 2003286103 A 20030804

Original IPC: A61F-13/02(B,I,H,US,20060101,20060824,A,L) A61K-31/4164(B,I,H,  
 US,20060101,20060824,A,L) A61K-31/445(B,I,H,US,20060101,20060824,A,F)

Current IPC: A61F-13/02(B,I,H,US,20060101,20060824,A,L) A61F-13/02(B,I,H,  
 US,20060101,20060824,C,L) A61K-31/4164(B,I,H,US,20060101,20060824,A,L) A61K-31/4164(B,I,H,  
 US,20060101,20060824,C,L) A61K-31/4174(R,I,M,EP,20060101,20060722,A) A61K-31/445(B,I,H,  
 US,20060101,20060824,A,F) A61K-31/445(B,I,H,US,20060101,20060824,C,F) A61K-47/06(R,I,M,  
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 EP,20060101,20051110,A) A61K-47/10(R,I,M,EP,20060101,20051110,C) A61K-47/12(R,I,M,  
 EP,20060101,20051110,A) A61K-47/12(R,I,M,EP,20060101,20051110,C) A61K-47/14(R,I,M,  
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EP,20060101,20051110,A) A61K-47/30(R,I,M,EP,20060101,20051110,C) A61K-47/44(R,I,M,  
EP,20060101,20051110,A) A61K-47/44(R,I,M,EP,20060101,20051110,C) A61K-9/70(R,I,M,  
EP,20060101,20051110,A) A61K-9/70(R,I,M,EP,20060101,20051110,C) A61P-13/00(R,I,M,  
WO,20060101,20060521,C) A61P-13/10(R,I,M,WO,20060101,20060521,A) C07D-233/00(R,I,M,  
WO,20060101,20060521,C) C07D-233/61(R,I,M,WO,20060101,20060521,A)

Current ECLA class: A61K-9/70E A61K-31/4174

Current US Class (main): 424-448000

Current US Class (secondary): 514-317000 514-396000

Original US Class (main): 424448

Original US Class (secondary): 514317 514396

Original Abstract: (Object) A transdermal preparation is provided, which ensures stable and effective absorption of 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197) which has a low skin absorption and is a bladder-selective muscarinic M<sub>3</sub> and M<sub>1</sub> receptor antagonist, into body through the skin while causing little side effects and providing sustained pharmacological effect with less skin irritancy.(Solving means) A composition comprising KRP-197 and an external preparation base is deposited and dried onto a structural body or a small pool of the composition is deposited on the structural body to obtain a single adhesive layer-type transdermal preparation or a reservoir-type transdermal preparation. These preparations can ensure high permeation of KRP-197 through the skin and sustained absorption of KRP-197 into body while causing decreased skin irritancy.

Claim: 1.\*\*\*1\*\*\*. A transdermal preparation containing a muscarinic receptor antagonist and an external preparation base.

## WIPO

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### \*\*TRANSDERMAL ABSORPTION PREPARATION PREPARATION POUR ABSORPTION TRANSDERMIQUE\*\*

Assignee: ~(except US)~ KYORIN PHARMACEUTICAL CO., LTD., 5, Kanda Surugadai 2-chome, Chiyoda-ku, Tokyo 1018311, JP Residence: JP Nationality: JP (KYOR) ~(only US)~ NAKASHIMA, Katashi, 14-19, Matsubara 2-chome, Tatebayashi-shi, Gunma 3740016, JP Residence: JP Nationality: JP ~(only US)~ OHMORI, Satoshi, 20-12, Yanagibashi-cho, Tochigi-shi, Tochigi 3280051, JP Residence: JP Nationality: JP ~(only US)~ KANAYAMA, Norihiro, 6095, Tomonuma, Nogi-machi, Shimotsuga-gun, Tochigi 3290101, JP Residence: JP Nationality: JP ~(only US)~ SAKAI, Yoshiki, c/o ONO PHARMACEUTICAL CO., LTD., 1-1, Sakurai 3-chome, Shimamoto-cho, Mishima-gun, Osaka 6188585, JP Residence: JP Nationality: JP

Inventor: NAKASHIMA, Katashi, 14-19, Matsubara 2-chome, Tatebayashi-shi, Gunma 3740016, JP Residence: JP Nationality: JP OHMORI, Satoshi, 20-12, Yanagibashi-cho, Tochigi-shi, Tochigi 3280051, JP Residence: JP Nationality: JP KANAYAMA, Norihiro, 6095, Tomonuma, Nogi-machi, Shimotsuga-gun, Tochigi 3290101, JP Residence: JP Nationality: JP SAKAI, Yoshiki, c/o ONO PHARMACEUTICAL CO., LTD., 1-1, Sakurai 3-chome, Shimamoto-cho, Mishima-gun, Osaka 6188585, JP Residence: JP Nationality: JP

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Language: JA (35 pages, 4 drawings)

Application: WO 2004JP11068 A 20040803 (Local application)

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Designated States: (National Original) AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW (Regional Original) AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

Original IPC: A61K-31/4174(A) A61K-9/70(B) A61K-47/06(B) A61K-47/10(B) A61K-47/12(B) A61K-47/14(B) A61K-47/30(B) A61K-47/44(B) A61P-13/10(B) C07D-233/61(B)

Current IPC: A61K-31/4164(R,A,I,M,EP,20060101,20060722,C) A61K-31/4174(R,I,M,EP,20060101,20060722,A) A61K-47/06(R,I,M,EP,20060101,20051110,A) A61K-47/06(R,I,M,EP,20060101,20051110,C) A61K-47/10(R,I,M,EP,20060101,20051110,A) A61K-47/10(R,I,M,EP,20060101,20051110,C) A61K-47/12(R,I,M,EP,20060101,20051110,A) A61K-47/12(R,I,M,EP,20060101,20051110,C) A61K-47/14(R,I,M,EP,20060101,20051110,A) A61K-47/14(R,I,M,EP,20060101,20051110,C) A61K-47/30(R,I,M,EP,20060101,20051110,A) A61K-47/30(R,I,M,EP,20060101,20051110,C) A61K-47/44(R,I,M,EP,20060101,20051110,A) A61K-47/44(R,I,M,EP,20060101,20051110,C) A61K-9/70(R,I,M,EP,20060101,20051110,A) A61K-9/70(R,I,M,EP,20060101,20051110,C) A61P-13/00(R,I,M,WO,20060101,20060521,C) A61P-13/10(R,I,M,WO,20060101,20060521,A) C07D-233/00(R,I,M,WO,20060101,20060521,C) C07D-233/61(R,I,M,WO,20060101,20060521,A)

Current ECLA class: A61K-9/70E A61K-31/4174

Original Abstract: [PROBLEMS] To provide a transdermal absorption preparation with little skin irritation whereby 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197), which is scarcely absorbed via the skin and has antagonism to bladder-selective muscarine receptors M3 and M1, can be continuously and efficiently absorbed into the body via the skin so that a sustained efficacy can be obtained while showing little side effects. [MEANS FOR SOLVING PROBLEMS] A transdermal absorption preparation is formed by flattening, drying or accumulating a composition comprising KRP-197 and an external preparation base to give a transdermal absorption preparation of the pressure-sensitive single layer type or a transdermal absorption preparation of the reservoir type. Thus, a preparation being excellent in the skin permeation of KRP-197 and sustained absorption thereof into the body and showing little skin irritation can be provided. L'invention a pour objet la mise au point d'une preparation pour absorption transdermique produisant un minimum d'irritation cutanee, le 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197) qui est difficilement absorbe par la peau et a un antagonisme envers des recepteurs de souris selectifs de la vessie M3 et M1, pouvant etre absorbe de facon continue et efficace par le corps a travers la peau de sorte que l'on peut obtenir une efficacite prolongee tout en limitant au maximum les effets indesirables. A cet effet, une preparation pour absorption transdermique est produite par stabilisation, sechage ou accumulation d'une composition comprenant KRP-197 et une base de preparation externe, pour obtenir une preparation pour absorption transdermique du type monocouche sensible a la pression ou une preparation pour absorption transdermique du type a reservoir. Ainsi, on obtient une preparation qui se caracterise par une excellente absorption cutanee de KRP-197 et une absorption prolongee par le corps, pour un minimum d'irritation

cutanee.

Derwent World Patents Index

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